

Supplementary Materials

Comprehensive assessment showed no association of variants at the *SLC10A1* locus with susceptibility to persistent HBV infection among Southern Chinese

Short title: *SLC10A1* variants and persistent HBV infection

Ying Zhang^{1,2,6,7,*}, Yuanfeng Li^{2,6,7,*}, Miantao Wu^{9,*}, Pengbo Cao^{2,6,7}, Xiaomin Liu¹⁰,
Qian Ren^{2,6,7}, Yun Zhai^{2,6,7}, Bobo Xie^{2,6,7}, Yanling Hu³, Zhibin Hu⁴, Jinxin Bei⁵, Jie
Ping^{2,6,7}, Xinyi Liu^{2,6,7}, Yinghua Yu⁸, Bingqian Guo^{2,6,7}, Hui Lu^{2,6,7}, Guanjuan Liu⁸,
Haitao Zhang^{2,6,7}, Ying Cui⁸, Zengnan Mo³, Hongbing Shen⁴, Yi-Xin Zeng⁵, Fuchu
He^{1,2,6,7}, Hongxing Zhang^{2,6,7}, and Gangqiao Zhou^{2,6,7}

¹School of Life Sciences, Tsinghua University, Beijing, China;

² State Key Laboratory of Proteomics, Beijing Proteome Research Center, Beijing
Institute of Radiation Medicine, Beijing, China;

³Center for Genomic and Personalized Medicine, Guangxi Medical University,
Nanning, Guangxi, China;

⁴Department of Epidemiology and Biostatistics, MOE Key Laboratory of Modern
Toxicology, School of Public Health, Nanjing Medical University, Nanjing, China;

⁵State Key Laboratory of Oncology in Southern China, Guangzhou, China;

⁶National Engineering Research Center for Protein Drugs, Beijing, China;

⁷National Center for Protein Sciences Beijing, Beijing, China;

⁸Affiliated Cancer Hospital of Guangxi Medical University, Nanning, Guangxi, China;

⁹State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China;

¹⁰Department of Laboratory Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China.

*These authors contributed equally to this work.

Correspondence should be addressed to:

Dr. Gangqiao Zhou, State Key Laboratory of Proteomics, Beijing Proteome Research Center, Beijing Institute of Radiation Medicine, 27 Taiping Road, Beijing 100850, P. R. China. E-mail: zhougq114@126.com; Phone: 86-10-66931204.

or

Dr. Hongxing Zhang, State Key Laboratory of Proteomics, Beijing Proteome Research Center, Beijing Institute of Radiation Medicine, 27 Taiping Road, Beijing 100850, P. R. China. E-mail: zhanghx08@126.com; Phone &fax: 86-10-61777099.

or

Dr. Fuchu He, State Key Laboratory of Proteomics, Beijing Proteome Research Center, Beijing Institute of Radiation Medicine, 27 Taiping Road, Beijing 100850, P. R. China. E-mail: hefc@nic.bmi.ac.cn; Phone &fax: 86-10-68177417.

Index

Supplementary Tables (see the attached Excel file):

Supplementary Table 1: Selected characteristics of the subjects involved in the present study.

Supplementary Table 2: The association results of genotyped and imputed SNPs in the Sample Set 1 (Guangxi population), the Sample Set 2 (GWAS population), and the pooled population.

Supplementary Table 3: The association results of haplotypes in the Sample Set 1.

Supplementary Table 4: Stratification analysis for genotyped and imputed SNPs by sex and age at diagnosis in the Sample Set 1.

Supplementary Table 5: Stratification analysis for haplotypes by sex and age at diagnosis in the Sample Set 1.

Supplementary Table 6: The association results of the low-frequency non-silent variation rs148467625 in the Sample Set 1.

Supplementary Table 7: Neutral theory test.

Supplementary Table 8: Association results of rs3133759 and rs13255741 in the Sample Set 2.

Supplementary Table 9: Primers used for genotyping the SNPs in *SLC10A1* with the Sequenom MassArray platform.

Supplementary Figures:

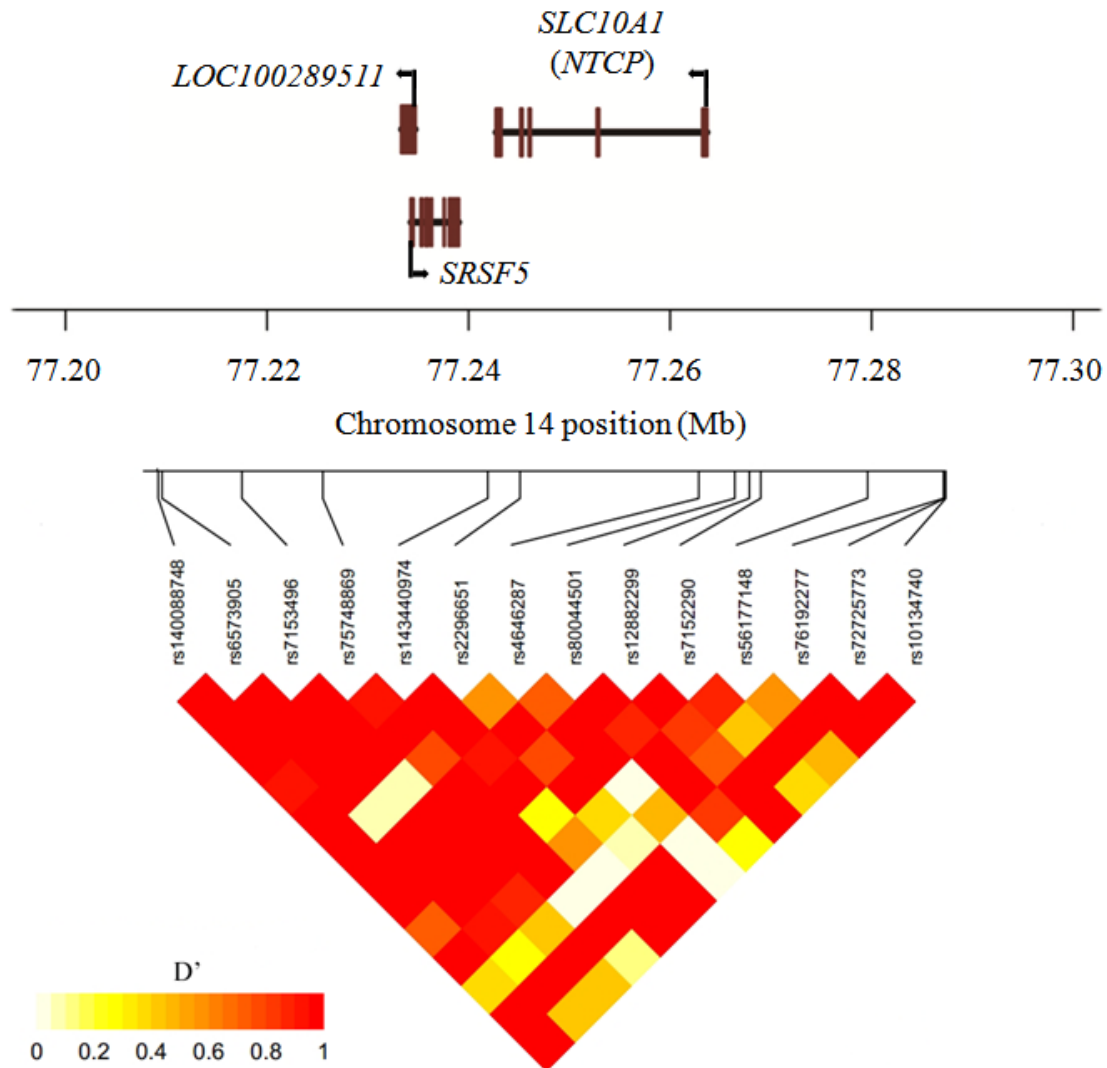
Supplementary Figure 1: Fourteen haplotype-tagging SNPs (htSNPs) in the *SLC10A1* region.

Supplementary Figure 2: The association results of genotyped and imputed SNPs in the Sample Set 1 (Guangxi population), the Sample Set 2 (GWAS population), and the pooled population.

Supplementary Figure 3: The known CNVs covering *SLC10A1* and its flanking region.

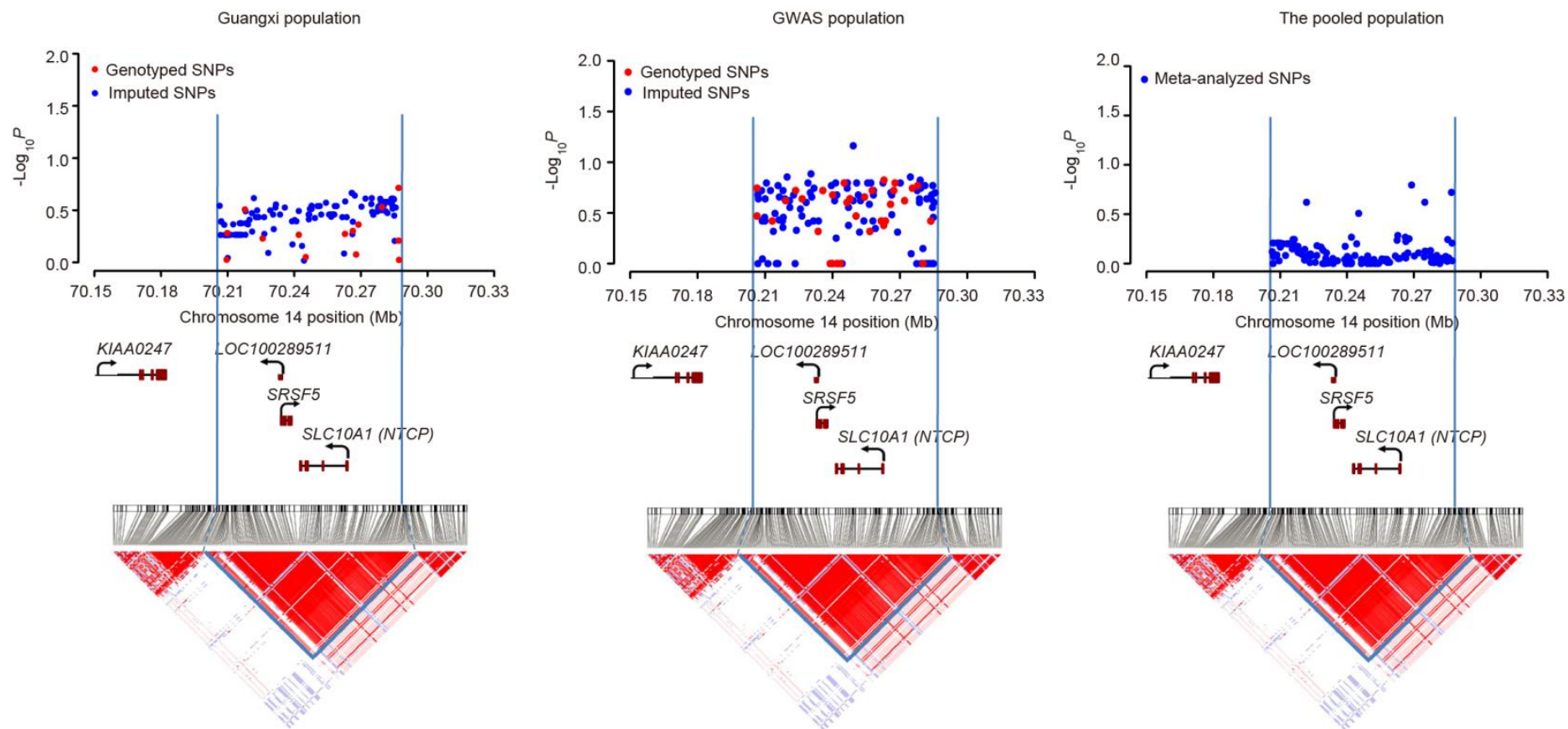
Supplementary Figure 4: Graphical scheme of eQTL obtained by ANOVA analysis in the liver tissues of 31 persistent HBV infected subjects (PIs).

Supplementary Figure 5: Power to detect a genetic effect of various sizes (OR = 1.1, 1.2, 1.3, or 1.4) versus study sample size.

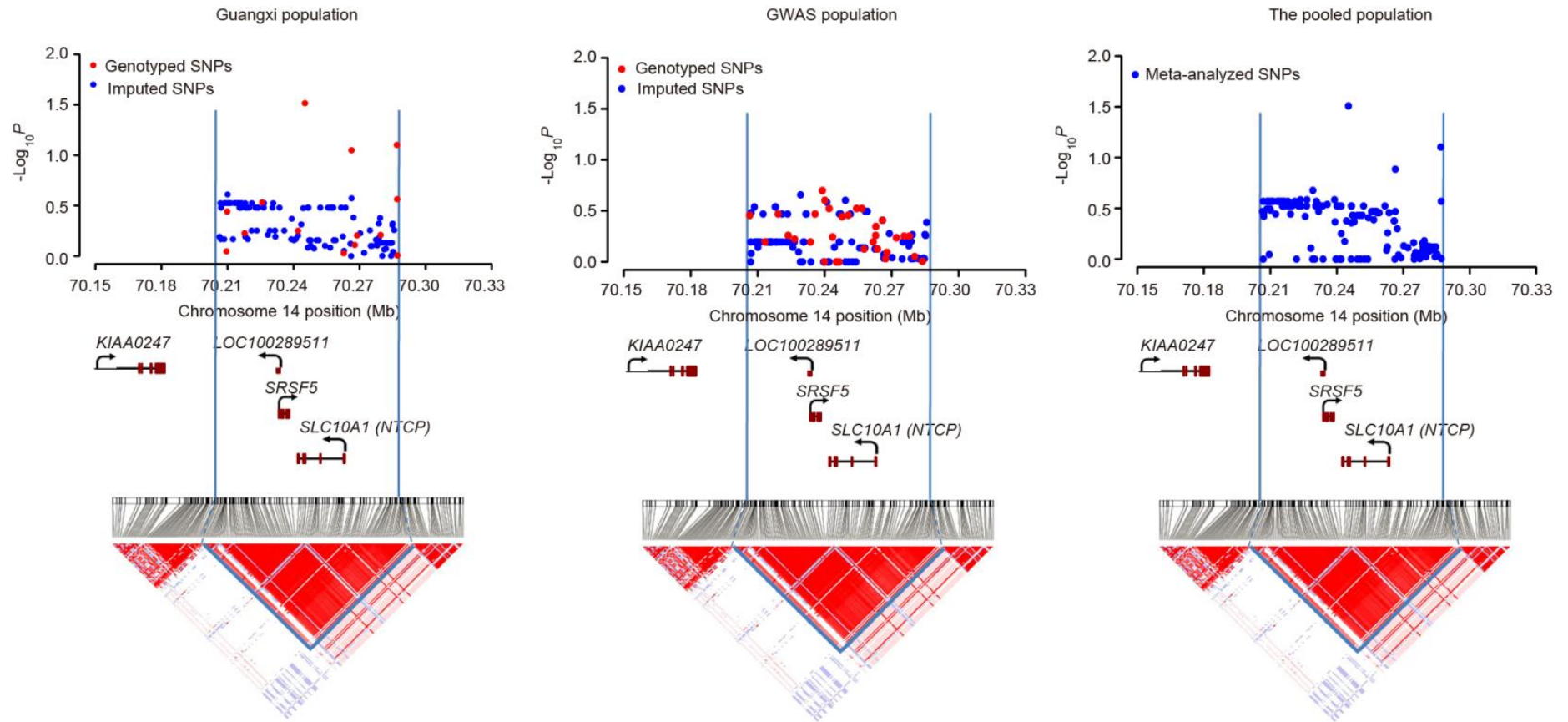


Supplementary Figure 1: Fourteen haplotype-tagging SNPs (htSNPs) in the *SLC10A1* region. Genomic locations of genes on the NCBI Build 37 human assembly were adapted from the University of California at Santa Cruz Genome Browser (<http://genome.ucsc.edu/>). The LD structure surrounding the *SLC10A1* gene in Chinese CHB and CHS samples of the 1000 Genomes Project was shown. Shading represents the magnitude and significance of pairwise LD (measured by D'), with a red-to-white gradient reflecting higher to lower LD values.

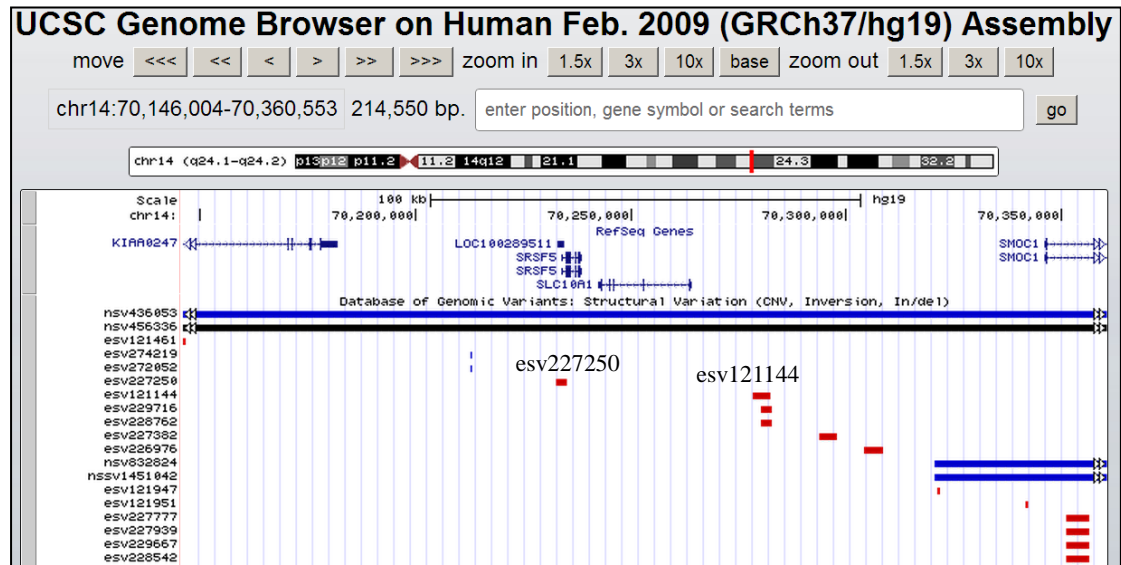
A.



B.

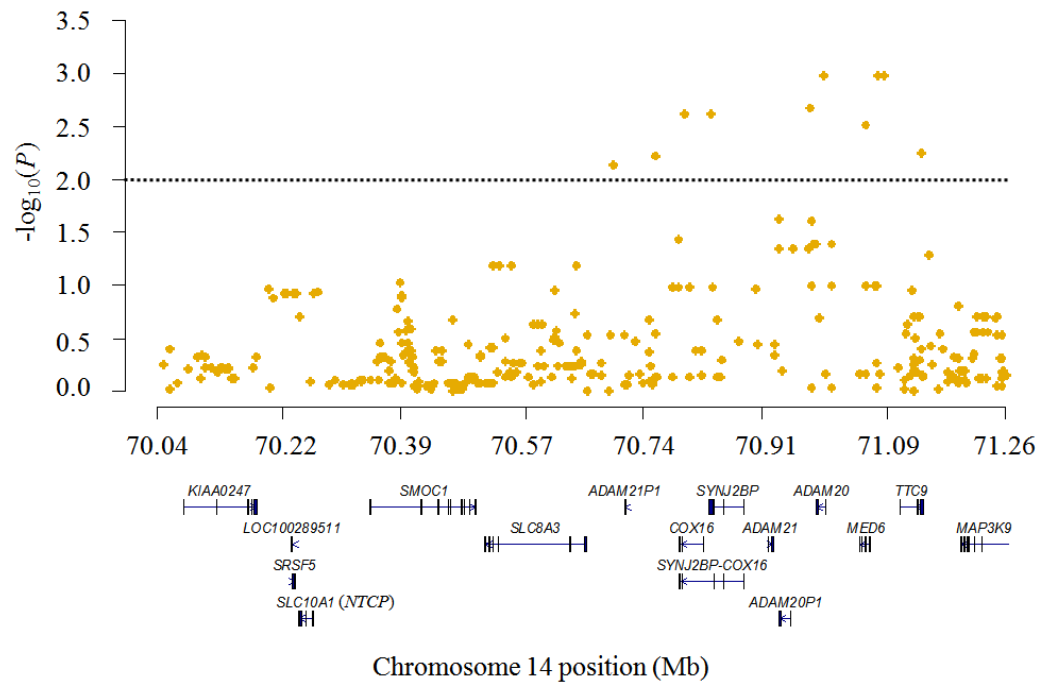


Supplementary Figure 2: The association results of genotyped and imputed SNPs in the Sample Set 1 (Guangxi population), the Sample Set 2 (GWAS population), and the pooled population. SNPs surrounding *SLC10A1* are plotted with their *P* values (shown as $-\log_{10}$ values) for dominant (A), and recessive (B) model tests as a function of genomic position (NCBI Build 37) in the Sample Set 1, the Sample Set 2, and the pooled population by meta-analyses. Genomic locations of genes on the NCBI Build 37 human assembly were adapted from the University of California at Santa Cruz Genome Browser (<http://genome.ucsc.edu/>). The LD structure surrounding the *SLC10A1* gene in Chinese CHB and CHS samples of the 1000 Genomes Project was shown. Shading represents the magnitude and significance of pairwise LD (measured by D'), with a red-to-white gradient reflecting higher to lower LD values. The most intense red spots have a $D'=1$.

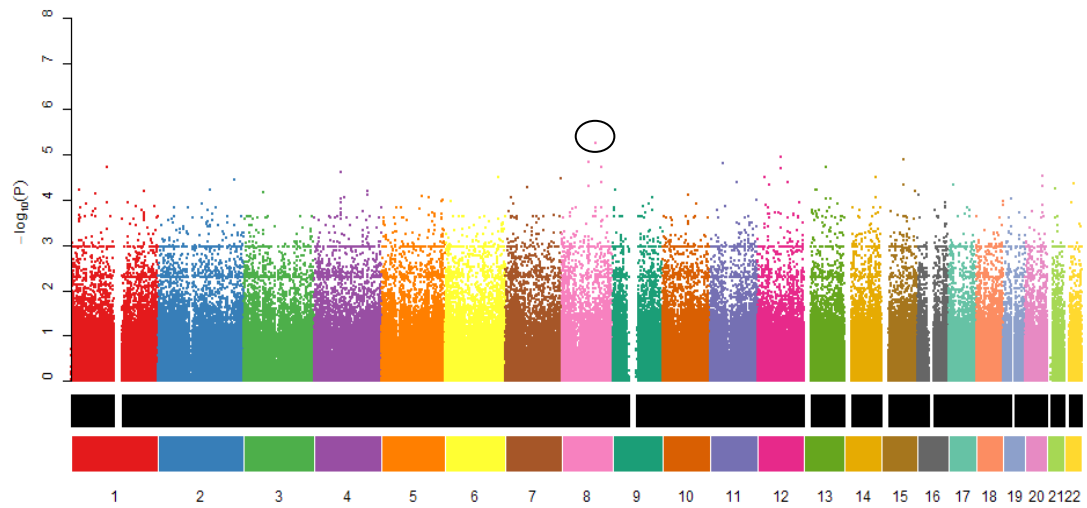


Supplementary Figure 3: The known CNVs covering *SLC10A1* and its flanking region. The nearest CNVs flanking *SLC10A1* documented in the database of genomic variants (DGV) were two deletions, of which one (esv227250, chr14:70232648-70235147, 2.5-Kb in length) located 7.4-Kb downstream and the other (esv121144, chr14:70278335-70282507, 4.2-Kb in length) 14.3-Kb upstream of *SLC10A1*. The figure was adapted from the University of California at Santa Cruz Genome Browser (<http://genome.ucsc.edu/>).

A.

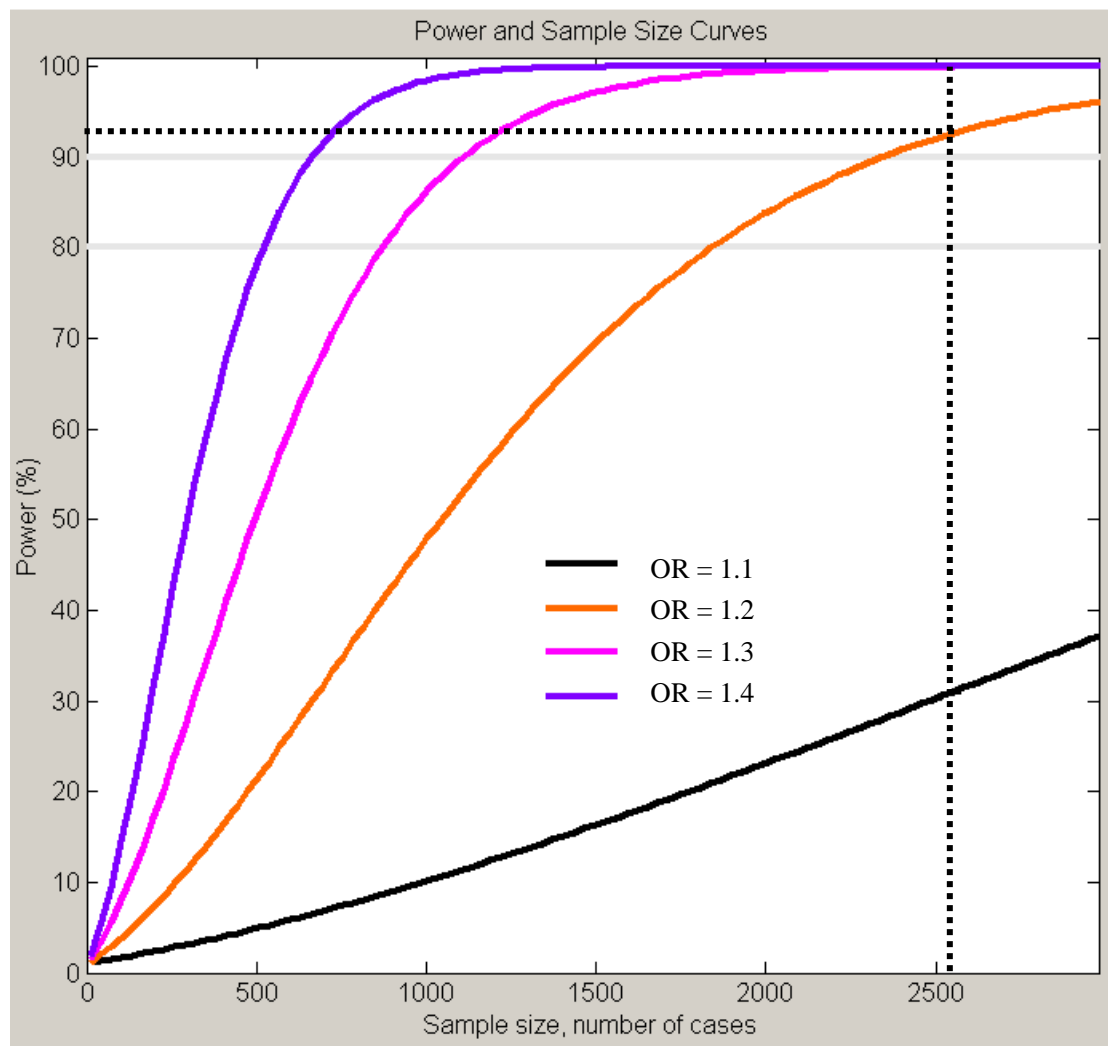


B.



Supplementary Figure 4: Graphical scheme of eQTL obtained by ANOVA analysis in the liver tissues of 31 persistent HBV infected subjects (PIs). A, Cis-eQTL analysis indicated that no SNPs within the 1-Mb upstream and 200-kb downstream of *SLC10A1* showed significant association ($P < 0.001$) with *SLC10A1* expression, with

10 SNPs showing marginally significance ($P < 0.01$). B, Trans-eQTL analysis indicated that no genome-wide significant trans-eSNPs ($P < 5.0 \times 10^{-8}$) were found, with only two SNPs rs3133759 and rs13255741 (the circled points) showing nominal significance ($P = 5.8 \times 10^{-6}$). The x-axis represents genomic position (NCBI Build 37), and the y-axis shows $-\log_{10}(P)$. Within each chromosome shown on the x-axis, the data are plotted from the p-ter end.



Supplementary Figure 5: Power to detect a genetic effect of various sizes (OR = 1.1, 1.2, 1.3, or 1.4) versus study sample size. Power is reported here as the probability of SNPs to be identified in a scan. Vertical and horizontal dashed lines show that the power of our pooled population (totally 2,550 cases and 2,124 controls), at significance level of 0.01, to detect an allele with a minor allele frequency (MAF) of 0.20 that confers an additive 1.2-fold effect on risk of persistent HBV infection, was estimated to be ~92%.